ANSWER 2 OF 2 USPATFULL SUMM . . . include arthritides, acquired immune deficiency syndrome (AIDS), burns, wounds such as bed sores and varicose ulcers, fractures, trauma, gastric ulceration, skin diseases such as acne and psoriasis, lichenoid lesions, epidermolysis bollosa, aftae (reactive oral ulcer), dental diseases such as periodontal diseases,. . . SUMM . . . and metastasis, AIDS, rheumatoid arthritis, gastric ulceration, burns, wounds such as bed sores and varicose ulcers, fractures, trauma, gastric ulceration, skin diseases such as acne and psoriasis, lichenoid lesions, epidermolysis bollosa, aftae (reactive oral ulcer), dental diseases such as periodontal disease,. . . the cornea in the case of an ulceration of the cornea, the DETD lungs in the case of lung cancer, the skin in the case of acne or psoriasis or skin diseases involving tissue destruction such as bed sores, varicose ulcers, etc. CLM What is claimed is: 1. A method of reducing of reducing a pathological excess of mammalian collagenolytic enzyme activity and an excessive degradation of connective tissue matrix protein components in a mammal in need thereof comprising: administering to said mammal a bisphosphonate in an amount which is. . . ACCESSION NUMBER: 97:66114 USPATFULL TITLE: Inhibition of the degradation of connective tissue

matrix protein components in mammals

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ANSWER 2 OF 2 USPATFULL L6 . . include arthritides, acquired immune deficiency syndrome SUMM (AIDS), burns, wounds such as bed sores and varicose ulcers, fractures, trauma, gastric ulceration, skin diseases such as acne and psoriasis, lichenoid lesions, epidermolysis bollosa, aftae (reactive oral ulcer), dental diseases such as periodontal diseases. . . SUMM . . . and metastasis, AIDS, rheumatoid arthritis, gastric ulceration, burns, wounds such as bed sores and varicose ulcers, fractures, trauma, gastric ulceration, skin diseases such as acne and psoriasis, lichenoid lesions, epidermolysis bollosa, aftae (reactive oral ulcer), dental diseases such as periodontal disease,. . . . . the cornea in the case of an ulceration of the cornea, the DETD lungs in the case of lung cancer, the skin in the case of acne or psoriasis or skin diseases involving tissue destruction such as bed sores, varicose ulcers, etc. CLM What is claimed is: 1. A method of reducing of reducing a pathological excess of mammalian collagenolytic enzyme activity and an excessive degradation of connective tissue matrix protein components in a mammal in need thereof comprising: administering to said mammal a bisphosphonate in an amount which is. . . ACCESSION NUMBER: 97:66114 USPATFULL TITLE: Inhibition of the degradation of connective tissue matrix protein components in mammals INVENTOR(S): Teronen, Olli Pekka, Kylanvanhimmankuja 9B, FIN 00640, Helsinki, Finland Sorsa, Timo Arto, Hakolahdentie 37 A 1, FIN 00200 Helsinki, Finland Salo, Tuula Anneli, Rantakoskelantie 5 B 9, FIN 90570 Oulu, Finland NUMBER DATE PATENT INFORMATION: US 5652227 19970729 APPLICATION INFO.: US 1995-380581 19950130 (8) DOCUMENT TYPE: Utility PRIMARY EXAMINER: Seidleck, James J. ASSISTANT EXAMINER: Cooney, Jr., John M. LEGAL REPRESENTATIVE: Browdy and Neimark NUMBER OF CLAIMS: 17 EXEMPLARY CLAIM: 1 NUMBER OF DRAWINGS: 5 Drawing Figure(s); 5 Drawing Page(s) LINE COUNT: 730 CAS INDEXING IS AVAILABLE FOR THIS PATENT. => d 2 clm L6 ANSWER 2 OF 2 USPATFULL What is claimed is:

said

CLM

1. A method of reducing of reducing a pathological excess of mammalian collagenolytic enzyme activity and an excessive degradation of connective tissue matrix protein components in a mammal in need thereof comprising: administering to

mammal a bisphosphonate in an amount which is effective in reducing the

matrix metalloproteinase (NMP) activity in said mammal.

- 2. The method of claim 1, which comprises administering to said mammal an effective amount of bisphosphonate which results in a significant reduction of the MMP dependent protein degradation in said mammal.
- 3. The method of claim 1, wherein said bisphosphonates comprises a bisphosphonate which is active as an inhibitor against at least one matrix metalloproteinase (MMP).
- 4. The method of claim 3, wherein said matrix metalloproteinase is selected from the group consisting of MMP-1, MMP-8 and a combination of MMP-1 and MMP-8, and wherein said mammal is a human having an increased level of MMP-1, MMP-8 or both MMP-1 and MMP-8.
- 5. The method of claim 1, wherein said bisphosponate is a geminal bisphosphonate having the general formula ##STR2## wherein R' and R" independently stand for a hydrogen or a halogen atom, a hydroxy, optionally substituted amino or optionally substituted thio group or an optionally substituted hydrocarbon residue.
- 6. The method of claim 5, wherein said bisphosphonate is selected from the group consisting of (1-hydroxyethylidene)bis-phosphonate, (dichloromethylene)bis-phosphonate (clodronate), (3-amino-1-hydroxypropylidene)bisphosphonate, (4-amino-1-hydroxybutylidene)bis-phosphonate, (6-amino-1-hydroxyhexylidene)bis-phosphonate, (1-hydroxy-2-(3-pyridinyl)ethylidene)bis-phosphonate, (3-(dimethylamino)-1-hydroxypropylidene)bis-phosphonate, (1-hydroxy-3-(methylpentylamino)propylidene)bis-phosphonate or a mixture thereof.
- 7. The method of claim 6, wherein said bisphosphonate is clodronate.
- 8. The method of claim 1, wherein said bisphosphonate is administered a way selected from the group consisting of oral, intravenous, parenteral, subcutaneous and topical administration.
- 9. The method of claim 1 wherein said mammal is a human selected from a populace susceptible to an excess degradation of connective tissue matrix protein components selected from the group consisting of diabetics and health care workers, and wherein said bis-phosphonate is administered prophylactically.
- 10. The method of claim 1 wherein said mammal is a human, with the proviso that such human is not (a) a patient in need of a skeletal marker in the form of .sup.99m technetium derivatives for diagnostic purposes in nuclear medicine, (b) a patient in need of administration

an anti-osteolytic agent, (c) a patient with ectopic calcification and ossification in need of an inhibitor of calcification, or (d) a patient in need of an anti-tartar agent.

11. The method according to claim 10 wherein said human is a patient selected from the group of patients in need of treatment of wounds, burns, fractures, lesions, ulcers, cancer and metastasis progression in connective tissues, rheumatoid arthritis and other arthitides, periodontitis, peri-implantitis, cysts, root canal treatment, AIDS, ulceration of the cornea, gastric ulceration, aftae, trauma, acne, psoriasis, loosening of end-osseal hip-protheses.

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- 12. The method according to claim 1, wherein said excessive degradation of connective tissue matrix protein components in mammals comprises a physiological or pathological condition selected from the group consisting of wounds, burns, fractures, lesions, ulcers, cancer and metastasis progression in connective tissues, rheumatoid arthritis and other arthitides, periodontitis, peri-implantitis, cysts, root canal treatment, AIDS, ulceration of the cornea, gastric ulceration, aftae, trauma, acne, psoriasis, loosening of end-osseal hip-protheses.
- 13. The method according to claim 1, wherein said excessive degradation of connective tissue matrix protein components in mammals comprises periodontitis.
- 14. The method according to claim 1, wherein said excessive degradation of connective tissue matrix protein components in mammals comprises peri-implantitis.
- 15. The method according to claim 1, wherein said excessive degradation of connective tissue matrix protein components in mammals comprises cancer and metastasis progression in connective tissues.
- 16. A method of inhibiting extracellular activity of MMP-1, MMP-8 or both MMP-1 and MMP-8, in a mammal in need thereof comprising: administering to said mammal a bisphosphonate in an amount which is effective in reducing the extracellular matrix MMP-1, MMP-8 or both MMP-1 and MMP-8 activity in said mammal.
- 17. A method according to claim 16 wherein said mammal is a human patient having an increased level of MMP-1, MMP-8 or both MMP-1 and MMP-8 and is in need of a treatment selected from the group consisting of treatments of wounds, burns, lesions, ulcers, rheumatoid arthritis

other arthritides, cysts, AIDS, ulceration of the cornea, gastric ulceration, aftae, trauma, acne and psoriasis.

or

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L7 ANSWER 18 OF 41 USPATFULL CLM What is claimed is:

1. A method of topically treating acne and other skin diseases which comprises administering to an individual a composition of a **fluoroquinolone** antibiotic present in a vehicle containing benzoyl peroxide, applied directly to the affected areas of the human skin.

- 2. A method described in claim 1 wherein the **fluoroquinolone** antibiotic is selected from a group consisting of, but is not limited to, ciprofloxacin, ofloxacin, enoxacin, cinoxacin, pefloxacin, lomefloxacin, norfloxacin, tosufloxacin, fleroxacin, temafloxacin, trovafloxacin, and difloxacin, in the form of an ointment, cream, lotion, liquid, gel, suspension, emulsion, cleansing bar, pledget, salve, tincture, spray, transdermal device or other appropriate non-toxic pharmaceutical vehicle.
- 3. The method described in claim 1 wherein the **fluoroquinolone** antibiotic is present in a range from about 5% to about 10% by weight

the composition.

- 4. The method described in claim 1 wherein the benzoyl peroxide is present in a weight percent from 2% to about 10% by weight of the composition.
- 5. A method described in claim 1 wherein the topical carrier is present in a weight percent from 75.0% to 94.9%.

ACCESSION NUMBER:

1999:67274 USPATFULL

TITLE:

of

Topical fluoroquinolone antibiotics combined with

benzoyl peroxide

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Weddington, Kevin E.

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